REMARKS

Claim 18 is amended herein by deleting the recitations of "arthrosteitis" and "rheumatic arthritis". In this regard, it is noted that Applicants did not intend to amend claim 18 in the previous Amendment filed January 31, 2008. "Arthrosteitis" and "rheumatic arthritis" were not previously recited in new claim 18 as presented in the Amendment filed September 4, 2007 and these conditions were deleted from claim 16 in the Amendment filed January 31, 2008. In view of the prosecution history of the present application, it is clear that claim 18 was presented in error in the Amendment filed January 31, 2008. Thus, Applicants respectfully request entry of the present Amendment to correct the inadvertent error to claim 18.

I. Response to Claim Rejections under 35 U.S.C. § 102

A. Kammer

The Office Action indicates that claims 18-21 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kammer (PTO-1449, June 24, 2005).

Claim 18 is amended herein by deleting the recitation of arthrosteitis and rheumatic arthritis as stated above, thereby rendering the rejection as to claims 18-21 moot.

Accordingly, Applicants respectfully request withdrawal of the §102 anticipation rejection.

B. Watkins

The Office Action indicates that claims 16 and 18-21 are rejected under 35 U.S.C. § 102(b) as being anticipated by Watkins (WO 02/30879 A2).

Applicants respectfully traverse the rejection and submit that Watkins does not contain an enabling disclosure and therefore the present invention is not anticipated.

In order for a prior art reference to be enabling and to thus anticipate a claimed invention, the reference must describe the claimed invention in sufficient detail to enable a person of ordinary skill in the art to carry out the claimed invention. The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. Thus, the mere disclosure of Watkins at pages 110-11 of the reference is not sufficiently enabling for the treatment of osteoarthritis since it does not provide any examples, direction or guidance for use of a specific HDAC inhibitor agent in the treatment of osteoarthritis. Additionally, as pointed out in the previous response, the references cited by Watkins in support of the assertion that HDAC inhibitors were known to treat inflammatory diseases such as osteoarthritis and rheumatic arthritis do not even mention these conditions and thus do not support the assertion made by Watkins.

Specifically, Watkins is not enabling for the use of HDAC inhibitor compounds in the treatment of osteoarthritis. Watkins discloses carbamic acid compounds and teaches that the compounds are useful as HDAC inhibitors, in particular, useful to inhibit proliferative conditions, such as cancer and psoriasis. The biological activity concretely disclosed in Watkins is merely a finding of "the ability to inhibit deacetylase activity and to inhibit cell proliferation" (cf. pages 230-247). Although Watkins describes reasons for usefulness for inhibiting proliferative conditions, such as cancer and psoriasis, in detail, the description about other uses is limited to the description at pages 110-111. At page 110, lines 15-18, it is described, "The compounds of the present invention may also be used in the treatment of conditions which are known to be mediated by HDAC, or which are known to be treated by HDAC inhibitors". But Watkins does not provide any additional guidance as to how the compounds can be used to treat

osteoarthritis other than the reference to Dangond et al and Takahashi and these references do not mention osteoarthritis.

The Examiner states that absent a specific statement in Watkins that the Dangond and Takahashi references are explicitly cited to show treating rheumatic arthritis/osteoarthritis was known, one cannot conclude that was the intent of Watkins. However, this is not the standard for evaluating a reference. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art. In considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. In this regard, it is apparent to one skilled in the art that the references Dangond and Takahashi are citations as support for the foregoing description in Watkins at page 111, lines 1-2, so that these two references should be taken into consideration: "Inflammatory disease (e.g., osteoarthritis, rheumatoid arthritis) (see, e.g., Dangond et al., 1998; Takahashi et al., 1996)." When viewed in the proper context, one skilled in the art would understand from the word "see" that the references cited are for reference and thus the findings relating to "inflammatory disease, osteoarthritis, rheumatoid arthritis" are described in the references cited after the word "see". Thus, it is clear that Watkins cites the Dangond and Takahashi references in support of the assertion that HDAC inhibitors were known to be useful in the treatment of inflammatory disease such as osteoarthritis. Otherwise, there would be no need to specifically cite these references separate from the other references cited in support of other conditions mentioned in the disclosure of Watkins.

As previously pointed out Dangond and Takahashi do not have any disclosure relating to the use of the compounds described therein in the treatment of osteoarthritis and inflammatory

disease. Dangond describes that "HDACs suggests they play a fundamental role in multiple and complex cellular pathways of immune system regulation" and Takahashi discloses that Trichostatin A inhibits IL-2 gene expression and has immunosuppressive activity and proliferation inhibiting activity. Thus, it is apparent that these disclosures do not establish a nexus between HDACs and osteoarthritis. Applicants have already explained that osteoarthritis is not a diseases relating to the immune system. See page 4, lines 1-5 of the Amendment filed on November 27, 2006 and the references referred to therein.

The Examiner indicates that it is Applicants' burden to rebut the presumption of operability of Watkins and states that the instant disclosure at page 6 indicates that it was known that HDAC inhibitors were used for rheumatic arthritis and osteoarthritis. However, Applicants disagree as to the Examiner's interpretation of the disclosure in the present specification. Specifically, at page 6 of the instant specification it is disclosed that a number of diseases are cited in patent reference 1, including rheumatic arthritis and osteoarthritis, but no specific effect is described and the basis which indicates a therapeutic effect is not shown. That is, the reference is not enabling for rheumatic arthritis and osteoarthritis. See the paragraph bridging pages 6-7 of the specification. Additionally, in the specification of patent reference 1, for the FK228 reduced form, a number of diseases are cited for the reason that the FK228 reduced form is effective for diseases induced by abnormal gene expression by its HDAC-inhibitory activity. Therein, although rheumatic arthritis and osteoarthritis are cited, any specific effect is not described and the basis which indicates a therapeutic effect is not shown. Thus, it is clear that the description in the present specification at page 6 referred to by the Examiner is to explain that the patent reference 1 is not enabling for rheumatic arthritis and osteoarthritis even though these conditions are mentioned therein.

Also, of all the references of record in the present application, including references cited in corresponding patent applications in foreign countries (which have been submitted in the present application in an Information Disclosure Statement), there is no reference which shows that osteoarthritis is "known to be mediated by HDAC" or "known to be treated by HDAC inhibitors". Accordingly, Watkins does not show the enablement for the use of HDAC inhibitor compound in the treatment of osteoarthritis.

The Examiner has not pointed to any other references in support of his position that Watkins is enabling for the treatment of osteoarthritis. The Examiner indicates that he has provided sufficient evidence that rheumatic arthritis was known to be treatable with HDAC inhibitors in view of Kammer. However, Kammer does not speak to osteoarthritis, which is recited in the present claims. Kammer teaches that an HDAC inhibitor (e.g. TSA) exhibits an effect whereby the expression of abnormal immune-related genes (CD154, IL-10, INF-gamma) in T cells of patients suffering from Systemic Lupus Erythermatosus is changed to a normal state, whereby the HDAC inhibitor is able to be used for treatment of many autoimmune diseases. Rheumatoid arthritis is shown as one of autoimmune diseases (e.g., claim 10).

As explained above, Dangood and Takahashi, which are cited in Watkins as references for inflammatory disease (e.g., osteoarthritis, rheumatoid arthritis), describe that the immunosuppressive activity is the base. Accordingly, each of these references indicates that the HDAC inhibitor acts on rheutmatoid arthritis through immunosuppressive activity.

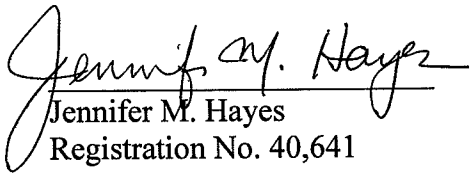
On the other hand, as described above, osteoarthritis is neither an autoimmune disease nor a disease in which CD154, IL-10, and INF-gamma participate. Accordingly, considering the functional mechanism of the HDAC inhibitor disclosed in the references, it is quite apparent that the use for osteoarthritis should be distinguished from the use for rheumatoid arthritis.

Moreover, even if Watkins describes osteoarthritis and rheumatoid arthritis in parallel, one skilled in the art who understood the contents of all of these references would not consider that the HDAC inhibitor can act on osteoarthritis through its immunosuppressive activity and rather would doubt its enablement. Thus, one skilled in the art would not consider to apply the HDAC inhibitor to osteoarthritis similar to rheumatoid arthritis.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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